REMARKS

This paper is filed in connection with an RCE request relating to application serial no. 09/698,787, originally filed on October 27, 2000, and claiming priority on a provisional patent application filed on October 29, 1999.

1. Summary of Interview Following Final Rejection.

Applicant thanks the examiner for the courtesy extended to applicant in an interview conducted on March 30, 2005. During that interview, a discussion occurred concerning why the last-most proposed amendment, filed after final rejection, was patentably distinguishable over the prior art of record. The examiner indicated that the proposed amendment raised new issues requiring additional consideration and/or search. For that reason, the proposed amendment was not entered. Applicant indicated that an RCE would be filed.

2. Supplemental Information Disclosure Statement.

Applicant apologizes for the delay in filing the RCE. However, since the interview, applicant conducted a supplemental search of the prior art and is submitting an updated information disclosure statement in connection with the RCE filing. Applicant makes no representations about the comprehensiveness of the search. The references identified in the search largely represent a text-based search of an electronic database for patents that make reference to items like "likelihood ratio" in the context of medical diagnostic systems. More importantly, applicant also submits a copy of a section from a medical book entitled "Basic and Clinical Biostatistics," published in or about 1994. This publication refers to the use of likelihood ratios in the context of revising prior probabilities, or pre-test odds, and is material to examination of the present application.

For the purpose of the public record, applicant wishes to emphasize that applicant is not claiming that applicant is the first to adapt Bayesian logic for the purpose of diagnosing an ailment. Applicant is the first, however, to adapt the purely statistically-based nature of Bayesian analysis to a web-based tool for doctors (or other users) that provides multiple potential diagnoses ("possible post-test diagnostic outcomes" in the claim language), all at the same time, and can rank the probabilities of the potential diagnoses, all at the same time. Leaving aside the fact that it is a better predictive tool, it is also better from the standpoint of the software programmer. The import of the latter point is that a Bayesian system is easy to change or amend without rewriting significant amounts of code. In short, it is better because it provides greater accuracy and because it is a more efficient approach for programming medical statistics. This point was not realized in the medical community before applicant's invention.

3. The Allowability of New Claim 12.

The biostatistics publication is an example as to how Bayesian statistical theory can be applied to predict the odds that a patient has a particular disease. Applicant has adapted Bayesian theory to a web-based system in a way that is distinguishable over the prior art of record, as described below. Specifically, new claim 12, which is similar in form to the last proposed amendment to claim 1 (not entered by the examiner), calls for a "web-based system" for diagnosing medical symptoms that includes, in part:

(1) "Statistically accrued data that is input from multiple sources via a common web-based system template"

* * *

(2) "the common template being used to generate a matrix that includes a plurality of possible post-test diagnostic outcomes"

* * *

(3) "each outcome indicating a possible disease and probability for that disease"

* * *

(4) "reporting the possible post-test outcomes to a user as a list of diagnostic probabilities ranked from the most likely to the least likely of possible diagnoses for a patient under examination"

* * *

(5) "each possible post-test outcome of the plurality of possible post-test diagnostic outcomes in the matrix being generated from an array of mathematical factors . . . with one of the factors being pre-test odds factors, and with each of the other factors in the array being input as an independent variable"

* * *

(6) "an independent variable is generated for each array for each possible post-test outcome of the matrix nearly simultaneously in response to each patient answer or test result"

With respect to the limitations indicated at (1)-(3) above, it is submitted that the prior art of record does not teach the use of a common web-based system template to generate a matrix that provides a plurality of possible post-test diagnostic outcomes, with each outcome indicating a possible disease and probability for that disease. Bear in mind that, mathematically speaking, the invention enables a display of ranked, possible diagnoses in a single "screenshot," if wanted.

In other words, it is possible to use the claimed invention to create a display that shows, all at the same time, which disease is most probable and which is least probably. For a physician, having a tool that immediately informs him or her that there is a 66% chance of angina (as a hypothetical example) with the next most likely disease being at a 20% chance, and so on, is an enormously powerful tool. Applicant has been unable to identify anything in the prior art of record that can produce this functionality. The invention claimed here provides that functionality. The prior art does not teach the reporting of diagnostic probabilities by ranking

them from most likely to least likely (claim 15). The mathematical implementation of the invention permits this type of display.

As indicated above, applicant concedes that the biostatistics publication teaches the claimed array in part (5) above when read alone. However, the examiner will appreciate that claim 12 is distinguishable in that it calls for a matrix that includes "a plurality of possible post-test diagnostic outcomes" (part (2) above) and therefore requires a plurality of arrays of mathematical factors, all at the same time – instead of a single array. More importantly, part (6) above calls for generation of an independent variable for each array nearly simultaneously in response to each patient answer or test result.

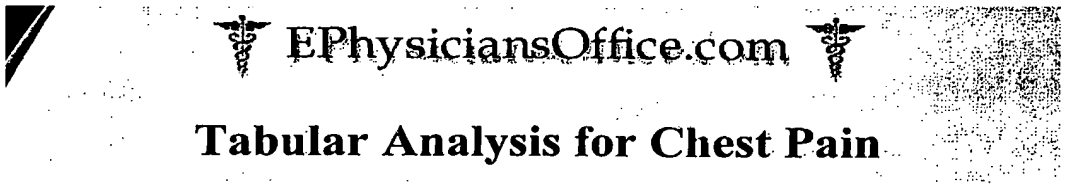
To further explain the above, applicant has adapted fundamental Bayesian theory in the way described in the biostatistics publication – except applicant has created a two-dimensional system, or matrix, where one event (*i.e.*, a patient answer to a question or a test result) may alter the diagnostic prediction for all of the possible disease probabilities in the matrix at the same time.

Each "array of mathematical factors," as claimed, essentially corresponds to a row of a matrix where the factors are multiplied together. Because the claim calls for "a plurality of possible post-test diagnostic outcomes," the matrix will likewise have a plurality of arrays or rows, each one of which consists of factors that are multiplied together, which is incorporated in the language of the claim (part (5) above).

The "pre-test odds" number is one factor in each array – and will be different for each array because disease probabilities (*i.e.*, "outcomes") vary from one disease to the next. These numbers are based on data accrued over time. The claimed "independent variables" are

generated from likelihood ratios (likelihood ratios are preferred according to the specification).[1] Every time a patient answers a question (or a test result is obtained), a likelihood ratio is generated from that event and is applied to each array, or row in the matrix, at the same time as a single independent variable that is multiplied against the pre-test odds number.

The number of independent variables is contingent on the number of questions or tests in the system and is therefore infinitely scalable (in other words, the array length is easy to expand). The significant point is: when a single question or test event occurs, it generates an independent variable that is a multiplier of the matrix. The value of that multiplier may well be different from one row to the next, because a separate likelihood ratio calculation is done as a subset calculation for each "disease" array, based on the single point of data provided by the answer or test result. This is conceptually illustrated in the table below and constructed as detailed in Figs. 10-14 of the patent specification:



(QUESTIONS/VARIABLES)

Angina/CAD	0.6667	1.15	1.15	1.15	1.3	0.7	1.15	1.3	2.5	1.0	1.0	77.52
GERD	0.0753	1.15	1.15	1.15	1.15	1.15	0.41	3	1.15	3	1.15	42.48
Peptic Ulcer	0.0101	3	2	3	2	1.5	1.0	1.0	1.0	1.0	1.0	35.29
Nonreflux Esophagitis	0.0204	1.15	1.15	1.15	1.15	3	4	1.0	1.0	1.0	1.0	29.98

[1] As it stands right now, claim 12 is not limited to the use of likelihood ratios. Likelihood ratios are specifically called for in dependent claim 13.

Tracheobronchitis/Asthma	0.0526	1.15	1.15	6	1.0	1.0	1.0	1.0	1.0	1.0	1.0	29.45
Esoph Spasm	0,0309	1.15	1.15	1.15	1.5	1.15	1.5	1.15	1.5	1.0	1.0	17.35
Miscellaneous musculo-skeletal chest wall	0.0204	1.5	1.5	3	1.0	1.0	1.0	1.0	1.0	1.0	1.0	12.1
Non-traumatic musculo-skeletal chest wall	0.0638	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	6
Anxiety	0.0526	1.15	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	5.7
Esoph Rupture	0.0101	1.15	1.15	1.15	1.15	1.5	1.5	1.5	1.0	1.0	1.0	5.62
Pneumonia	0.0417	1.15	1.15	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	5.22
Pericarditis	0.0204	1.15	2	1.15	1.0	1.0	1.0	1.0	1.0	1.0	1.0	5.12
Aortic Dissection	0.0101	1.15	1.15	1.15	1.15	1.5	1.5	1.0	1.0	1.0	1.0	3.82
Traumatic musculo-skeletal chest wall	0.0309	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	3
Pancreatitis	0.0101	1.15	1.15	2	1.0	1.0	1.0	1.0	1.0	1.0	1.0	2.6
Mitral Valve Prolapse	0.0101	1.5	1.5	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	2.22
Superficial Lesions	0.0204	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	2
Pulmonary Thromboembolism	0.0101	1.15	1.15	1.15	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.51
Pneumothorax	0.0101	1.15	1.15	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.31
Shingles	0.0101	1.15	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.14
		LR	LR	LR	LR	LR	LR	LR	LR	LR	LR	

PRE-TEST ODDS

LR = LIKELIHOOD RATIOS

POST-TEST PROBABILITY

Pre-test odds x LR x LR x LR . . . = post-test odds (converted to post-test probability)

Referring to the above table, which represents a diagnostic event where a patient enters a hospital with a single complaint (chest pain), the top row corresponds to one possible post-test diagnostic outcome, "angina." The table, as a whole, reflects a 20-row matrix, each row corresponding to different possible post-test diagnostic outcomes (angina, GERD, peptic ulcer, etc.). According to the table, any patient walking into a hospital complaining of chest pain (prior to being subjected to any diagnostic tests or questions) has pre-test odds of .667 for angina

(essentially 40% probability of a heart attack). That number is based on accrued statistics and is purely a statistical fact based on past data. Likewise, pre-test odds for GERD are .0753, pre-test odds for peptic ulcer are .0101, and so on, for each listed possible post-test diagnostic outcome.

Upon answering a single question or obtaining a single test result, and depending on the particular answer or result, a likelihood ratio is generated for each possible outcome (or, for each one of the 20 possible diseases in the matrix). This is reflected in the second column of the above table (the first column to the immediate right of the pre-test odds column). Depending on the answer or test result, in some cases, the likelihood ratio resulting from the patient's answer to a question or a test result will alter pre-test odds upwardly (*e.g.*, 1.15); in some cases, pre-test odds will be altered downwardly (*e.g.*, .85); and in some cases, pre-test odds will remain unchanged (*e.g.*, 1.0).

As applicant previously indicated in applicant's proposed post-final amendment, one way to think of a likelihood ratio is that it takes into account that a patient's answer to a question or a test result is not necessarily absolute. Each piece of information is statistically applied to predict a possible disease by using likelihood ratios. A person who complains of chest pain may, for example, be asked the question, "Do you smoke?" If the answer is "yes," then likelihood ratio analysis creates an input variable that has a value that is greater than "1" and therefore functions as an "upward" multiplier in the "angina" array. For example, it is well-known today that people who smoke are more likely to have heart attacks. The likelihood of that fact can be estimated statistically based on prior data to generate the likelihood ratio.[2]

[2] In accordance with the invention, it is possible to update data for calculating pre-test odds or likelihood ratios on an ongoing basis.

The same answer ("yes") to the same question ("Do you smoke?") may lead to a different likelihood ratio, and hence, a different input variable for another disease. As a purely hypothetical example, statistical analysis may prove that smoking makes people less anxious or has no impact at all on a person's anxiety level (*see* row "9" in the above table). In the former case, a likelihood ratio of "less than 1" would be generated. When multiplied against the "pre-test odds" for anxiety, it would therefore decrease the predicted post-test probability that a patient is suffering from anxiety as a result of complaining about chest pain. If the statistical answer to the question is "neutral," then the likelihood ratio is "1." When used as a multiplier in an array, it therefore does not alter the pre-test odds at all.[3] For an additional explanation, applicant refers the examiner to pages 10-12 of applicant's Amendment and Response After Final Rejection, mailed to the USPTO on March 7, 2005.

While applicant concedes that the use of Bayesian logic is known in the prior art, no one has applied Bayesian logic in the two-dimensional way described above, which is now reflected in independent claim 12. This is a unique form of predictive modeling in a number of respects.

First, a matrix or multi-dimensional array, as described above, enables a complete series of potential diagnoses for all potential diagnoses based on a single symptom. In contrast, the prior art tends to focus on making a single diagnosis, one at a time, moving sequentially from one potential diagnosis to the next, as test results are obtained or patient questions are answered. This approach follows the "rules-based" concept outlined in earlier papers. The present invention reaches an answer for all potential diagnoses at the same time. Every time a likelihood ratio is calculated it has the potential to alter all diagnoses in the matrix.

---

[3] The table, which is purely hypothetical, illustrates "1.15" in the second column of row "9." Statistical analysis may establish that people who smoke are predisposed toward anxiousness. The beauty of this type of analytical system is that statistics remove subjective judgments.

Second, the claimed matrix provides a mathematical model that is much more adaptable than pure rules-based systems. This form of predictive tool enables the user to create additional likelihood ratios in a self-expanding way without requiring significant reprogramming.

Third, accrued data enables both pre-test odds numbers and likelihood ratios to evolve automatically. The underlying power of the invention is that this evolution can be subtle over long periods of time – in the same way that averages adjust slowly when large populations are involved in making the averages. Or, the evolution can be more abrupt: as an example, if a new, definitive test is developed for a particular disease, it is easy to add another likelihood ratio column in the table illustrated above that will generate a very high multiplier in the array (or row) relating to that disease, without having a large amount of statistically accrued data from other patients.[4] Perhaps the most meaningful difference between the claimed invention and the prior art is that it simply provides a better statistical model for predicting diseases that is more adaptable and becomes more accurate in time. As indicated previously, it is purely based on statistical analysis.

In past remarks submitted by the applicant, applicant has pointed out the difference between "evidence-based systems" and "rules-based systems." While all predictive tools are based on the accrual of evidence, rules-based system are more dependent on logical branch-tree analyses that are a combination of a doctor's experience coupled with programming logic. This is directly related to the "if-then" logic involved in prior art systems. The importance of that type of logical approach to the predictive outcome is minimized in the present invention.

---

[4] Once again, the likelihood ratio multiplier for other diseases could be "1" because that particular test is meaningless relative to other diseases.

Applicant notes the receipt of the examiner's advisory action that indicates entry of applicant's prior declaration in the record. While applicant understands that the proposed claim amendments (filed March 7, 2005) were not entered, applicant respectfully requests that the examiner review applicant's prior remarks relating to the support in the specification for the claim limitations described above. In particular, applicant's remarks submitted in applicant's paper entitled "Amendment and Response After Final Rejection," dated on or about March 7, 2005, pointed to the various parts of the specification that supported the predecessor version of claim 12 – the claim not being entered by the examiner because it raised new issues requiring search. If the examiner has further questions regarding these issues, applicant respectfully requests the opportunity to respond prior to entry of a final rejection.

For the foregoing reasons, applicant respectfully requests allowance of the claims in this case.

Respectfully submitted,

VICTOR LEVY

By: Bruce A. Kaser

Bruce A. Kaser
Registration No. 31,531
DAVIS WRIGHT TREMAINE LLP
2600 Century Square
1501 Fourth Avenue
Seattle, WA 98101-1688
Telephone: (206) 628-7653

I, Bruce A. Kaser, hereby certify that this document and its attachments are being deposited with the U.S. Postal Service as First Class Mail, postage prepaid, in an envelope addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 31 day of May, 2005.

Bruce A. Kaser
Name (signature)